

FAST FACTS

Eltrombopag Treatment of Thrombocytopenic Subjects with Advanced Myelodysplastic Syndrome (MDS), Secondary Acute Myeloid Leukemia After MDS (sAML/MDS), or de novo AML

Sponsor: GlaxoSmithKline

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Study Title: PMA112509, a Phase I/II Study of Eltrombopag in Thrombocytopenic Subjects with Advanced Myelodysplastic Syndrome (MDS) or secondary Acute Myeloid Leukemia after MDS (sAML/MDS)

Subject Population: Advanced MDS
Secondary AML after MDS (sAML/MDS)
De Novo AML
(Relapsed, refractory or ineligible to receive azacitidine, decitabine, intensive chemotherapy, autologous/allogeneic stem cell transplantation.)

Currently accepting participants? *Yes*

This is a randomized, placebo-controlled, multi-center study to assess the safety and tolerability of eltrombopag in thrombocytopenic subjects with advanced MDS, Secondary Acute Myeloid Leukemia after MDS (sAML/MDS), and De Novo AML. Subjects must be relapsed, refractory, or ineligible to receive azacitidine, decitabine, intensive chemotherapy or autologous/allogeneic stem cell transplantation.

This is a placebo-controlled study in which patients will receive study medication daily for 6 months, during which time the dose of study medication may be adjusted based upon individual platelet counts and bone marrow blast counts. All subjects will be permitted to receive local standard of care (platelet transfusions, mild chemotherapy, cytokines, valproic acid, all-trans retinoic acid, ESAs or G-CSF) in addition to study medication.

If an Internal Safety Review Committee (iSRC) determines that a statistically and clinically significant decrease in bone marrow blast counts is seen in subjects treated with eltrombopag as compared to placebo, it may recommend that placebo subjects crossover to eltrombopag treatment.

Who can participate?

(See protocol for additional inclusion criteria)

- Subjects with advanced MDS, sAML/MDS, or de novo AML with $\geq 10\%$ and $\leq 50\%$ blasts in bone marrow. Peripheral blood blast change over time should not be suggestive of highly proliferative disease (as judged by the investigator). Must have stable disease indicated by a doubling of peripheral blast counts >7 days during screening.
- Men and women over the age of 18.
- Platelet Transfusion dependent or have a platelet count taken within the 4 weeks prior to randomization that is <30 Gi/L. Must have data to confirm this for 4 weeks prior to randomization.
- Prior therapy with demethylating agents (azacitidine or decitabine), lenalidomide or IL-11(oprelvekin) must have been completed at least 4 weeks before Day 1 (wash-out period does not apply discontinued the therapy due to lack of efficacy).
- Antithymocyte/antilymphocyte globulin, intensive chemotherapy, or autologous/allogeneic stem cell transplantation must have been completed at least 2 months before Day 1 (wash-out period does not apply discontinued the therapy due to lack of efficacy)..
- Baseline bone marrow examination including the following:
 - a. cytomorphology to confirm bone marrow blasts between 10-50%
 - b. cytogenetics (provide only most prevalent abnormal clone)
- Prothrombin time (PT/INR) and activated partial thromboplastin time (aPTT) must be within 80 to 120% of the normal range at baseline.
- Standard of care (SOC) treatment allowed: (e.g. blood transfusions, administration of cytokines, palliative chemotherapy, valproic acid, all-trans retinoic acid etc.) will be allowed at any time if clinically indicated for all subjects in both arms of the study.

Ineligible Subjects:

(See protocol for additional exclusion criteria)

- History of treatment for cancer (other than MDS, sAML/MDS, or de novo AML) with systemic chemotherapy and/or radiotherapy within the last 2 years.
- History of treatment with romiplostim or other TPO-R agonists.
- Bone marrow fibrosis that leads to an inability to aspirate marrow for assessment.
- Spleen size >14 cm (length as per ultrasound examination).
- Leukocytosis $\geq 25,000/uL$ prior to Day 1 of study medication.
- Subjects infected with Hepatitis B, C or Human Immunodeficiency Virus (HIV).

- Subjects with liver cirrhosis.

Detailed Study Description:

Eltrombopag is an orally available, small molecule thrombopoietin receptor agonist that is approved as a treatment for chronic idiopathic thrombocytopenic purpura (ITP) to increase platelet counts. The present study is designed to evaluate the safety and tolerability of eltrombopag, initially administered as 50 mg oral tablets once daily in adult thrombocytopenic subjects with advanced myelodysplastic syndrome (MDS) or secondary acute myeloid leukemia after MDS (sAML/MDS).

Standard of care (SOC) treatment (e.g. blood transfusions, administration of cytokines, palliative chemotherapy, valproic acid, all-trans retinoic acid etc.) will be allowed at any time if clinically indicated for all subjects in both arms of the study.

Disease status will be evaluated by means of bone marrow examinations every 3 months.